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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/970,649	10/05/2001	Monica Jonsson	003300-833	2032

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/970,649	JONSSON ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37,60-75 and 77-113* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-37,60-75 and 77-113* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed April 3, 2006 have been entered. Claims 97-113 have been added. Claims 1-37, 60-75, and 77-113 are pending.

Upon reconsideration, the outstanding rejection under 35 USC 103(a) is withdrawn. A new ground of rejection is set forth below.

The outstanding rejection under 35 USC 112, first paragraph is withdrawn in view of the remarks in applicant's response filed April 3, 2006.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-37, 60-75, and 77-113 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO97/14408 ('408) in view of Laasko et al. and Woiszwillo et al., references of record.

'408 teaches a process of making a sustained released parenteral microparticles encapsulated with starch by mixing the starch with the biologically active substance, insulin or BSA, and then mixing it with aqueous polyethylene glycol solution. '408 also teaches the concentration of polyethylene glycol as 20% or 40% and its average loecular weight as 20000. After stirring for 24 hours below 50°C, microparticles are formed. '408 further teaches the coating of the starch microparticles containing biologicals with PLGA using air-suspension technique (see page 12, lines 15-20, pages 14-15, Examples 1-3, pages 15-17, Examples 4-6). '408 further teaches modified starch, such as those dissolved by α-amylase, can be used (see page 7, line34 bridging page 8, line 6). '406 also teaches the particle size produced is in a range of 10-200μm, 20-100μm, 10-60 μm, or 40-60μm (See page 7, lines 28-33). '408 also teaches the drying processes for the starch particles as freeze-drying, spray-drying or vacuum drying (See page 9, lines 7-8).

'408 does not expressly teach the method of mixing the polyethylene glycol solution with the biologically active substance before mixing with the aqueous starch solution. '408 does not expressly teach the herein claimed characteristics (i.e., nitrogen content, particle size, and amylopectin content) of starch employed. '408 does not expressly teach the biologically active substance as human growth hormone, '408 does not expressly teach the herein recited temperature employed during the mixing process between starch solution and the polyethylene glycol-biological actives solution.

Woiszwillo et al. teaches a method of preparing biological active microparticles suitable for parenteral administration by mixing an aqueous solution of bioactive

compounds, such as insulin, leuprolide, and bovine Serum Albumin, with the solution of polyethylene glycol. (See col. 21, line 11-34; also col. 5, line 65 - col.7, line 49). Woiszwillo et al. also teaches the biological active substances as enzymes, recombinant proteins, polypeptide, carbonhydrate, such as insulin, leuprolide, and human growth hormone (See col. 7, line 50 – col. 8, line 32). Woiszwillo et al. also teaches the solution of preferred polymers, including polyethylene glycol, having molecular weight of 3,000 to 500,000 daltons can be added to the solution of the macromolecules in order to form a microparticles (See col. 12, lines 33-42). Woiszwillo et al. also teaches the way to optimizing the microparticles by altering the particle size and temperature (See col. 13, lines 30-36).

Laakso et al. teaches polyacryl starch is suitable as carrier for passive target drug delivery since polyacryl starch is rapidly taken up by the reticuloendothelial system (RES) (see the abstract). Laakso et al. also teaches the nitrogen content of polyacryl starch can be affected by the amount of initiator employed (See the abstract and figure 2 in page 964). Laakso et al. teaches the degradation of polyacryl starch can be affected by the amount of initiator employed and the degree of derivatization of the starch (See particularly the abstract and page 966-967, Discussion Section).

It would have been obvious to one of ordinary skill in the art at the time of invention to mix the polyethylene glycol solution with the biologically active substance before mixing with the aqueous starch solution. It would have been obvious to one of ordinary skill in the art at the time of invention to employ the suitable starch compounds herein claimed in the method of preparing the herein claimed microparticles. It would

have been obvious to one of ordinary skill in the art at the time of invention to employ the cited prior arts' method for encapsulating human growth hormone.

One of ordinary skill in the art would have been motivated to mix the polyethylene glycol solution with the biologically active substance before mixing with the aqueous starch solution since the resulting mixture of starch solution, aqueous PEG solution, and aqueous biologically active substance solution would be essentially the same regardless the order of mixing the three solution (i.e., mixing A+B, then adding C would be essentially the same as mixing B+C, then adding A), absent evidence to the contrary. Furthermore, Woiszwillo et al. clearly teaches the mixing of biologically active substances with polyethylene glycol solution first.

One of ordinary skill in the art would have been motivated to employ the suitable starch compounds herein claimed in the method of preparing the herein claimed microparticles since the polyacryl starch is well-known as useful for passive targeting drug delivery. Optimizing the nitrogen content, molecular weight, the starch solution concentration, the weight ratio between the biological active substance and starch, the temperature employed, and particle size would be considered obvious as being within the purview of skilled artisan. Optimizing the temperature of mixing the starch solution and the polyethylene biological actives would be obvious since cooling down the starch solution will avoid degradation of the biological actives due to the sensitive nature of the proteins and/or peptide.

One of ordinary skill in the art would have been motivated to employ the cited prior arts' method for encapsulating human growth hormone since the method

suggested in the cited prior arts are used to encapsulate sensitive biological actives, such as insulin and proteins. Woiszwillo et al. clearly teaches other proteins or peptides, such as human growth hormone, may be used. Therefore, substituting the insulin or BSA with human growth hormone in the method of preparing the sustain release parenteral microparticles would therefore be considered as simple selection over obvious alternatives.

Response to Arguments

Applicant's arguments with respect to claims 1-37, 60-75, and 77-113 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1617